REMARKS

I. STATUS OF CLAIMS

By this Amendment, new claims 17 through 20 have been added. Support can be found throughout the specification and claims as originally filed, including in the specification at page 1, lines 9-13, and pages 22-27. No new matter has been added.

Claims 9-20 are now pending.

II. INTERVIEW SUMMARY RECORD

Applicant thanks Examiner Seeman for her time conducting a telephonic interview on August 30, 2005, with his undersigned representative. The claims and pending rejections were discussed, and the Examiner indicated that the rejection of claims 11 and 12 under 35 U.S.C. § 112, first paragraph would be reevaluated if these claims were presented in independent form.

Accordingly, Applicant presents herein independent claims 17 and 18, which contains recitations similar to those of previously presented claims 11 and 12. For example, claims 17 recites, *inter aliai,* "A method of chronic gastritis caused by urease..." and claim 18 recites, *inter aliai*, "A method of treating a gastroduodenal ulcer caused by urease..." Additionally, Applicant presents herein independent claims 19 and 20, which contain similar recitations but are more specifically relate to the subject matter of claim 16.

III. REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 9-16 were rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking sufficient written description and enablement. (Office Action, pg. 4-8.) Applicant respectfully traverses for at least the following reasons.

In essence, claims 9-16 appear to have been rejected because the Office is viewing them as being improperly directed to "mechanisms of action" and not well defined specific conditions. (*E.g.,* Office Action, pg. 4 ("Modulation of a receptor involves antagonism, inhibition, agonism and others... It is not seen where the instant specification adequately describes the nexus between the modulation of urease activity and a useful treatment of a single disease or condition."); pg. 8 ("claims directed to mediating a biological pathway are devoid of identifiable utility and are therefore not useful.").)

However, the Office does not cite any applicable legal basis in support of these rejections. Therefore, even if properly characterized, the absence of a nexus with "a useful treatment of a single disease or condition" is not a proper rejection under Section 112, first paragraph.

Moreover, even if the legal theory is correct, the claims have been incorrectly characterized as being merely "directed to mediating a biological pathway." They are, in fact, directed to the treatment of specified conditions. Thus, as discussed further below, the factual premise of the rejections, that the application does not describe a "nexus between the modulation of urease activity and a useful treatment of a single disease or condition" is incorrect. Indeed, the Office itself has recognized such a nexus.

In addition, contrary to the Office's characterization, the specification provides express guidance as to what is encompassed by gastric mucosa injury other than ulcers. Indeed, several of the claims expressly refer to, among other things, chronic gastritis.

These several issues are discussed further below.

i) The claims have been mischaracterized -- they are not merely "directed to mediating a biological pathway"

Claim 9, as one example, is directed to "[a] method of treating gastric mucosa injury caused by urease," as more specifically set forth in the claim. Thus, on its face, it is directed to treatment of conditions ("gastric mucosa injury") and not merely a biological pathyway. This is reinforced in claims 11 and 12, which recite that "the gastric mucosa injury comprises chronic gastritis" and "the gastric mucosa injury comprises gastroduodenal ulcer," respectively. Similarly, as more specifically set forth in the above amendments, independent claims 17-20 recite methods of treating chronic gastritis and gastroduodenal ulcer.

Thus, the claims are expressly directed to treatment of conditions and not merely biological pathways, as characterized by the Office. The Office's characterization of all of the claims as being "drawn to the treatment of any and all diseases that are treatable by treating gastric mucosa injury caused by urease" (Office Action, pg. 7) is likewise inaccurate.

For at least the reason that the present rejections depend upon these inaccurate characterizations, they should be withdrawn.

ii) The premise of the rejections, that the application does not describe a "nexus between the modulation of urease activity and a useful treatment of a single disease or condition" is incorrect

In support of the written description rejection, it is contended that "[t]he instant specification does not adequately describe the nexus between the modulation of the urease activity and a useful treatment of a disease/condition." (Office Action, pg. 4.) This is factually incorrect, and contradicted by the Office's express recognition that the application discloses, *in detail*, a causal relationship between the *H. Pylori* and mucosa injury.

In particular, on page 3 of the Office Action, the Office accurately and extensively quotes from the present specification. The quoted disclosure provides, among other things and as more specifically set forth in the specification taken as a whole, that (1) urease hydrolyzes urea to produce ammonia, (2) ammonia has a strong mucosa injurious effect, causing, among other things, neutralization of gastric acid, (3) thereby enabling habitation of *H. Pylori*, (4) ultimately causing cell injury. (Specification, pg. 1.) The Office expressly relies upon this disclosure to demonstrate the casual relationship between *H. Pylori* and mucosa injury, concluding, based on this disclosure, that

> The bacteria (H.Pylori) starts a chain reaction which creates high acidity in the stomach. This high level of acidity damages mucosa. The ucler is caused by this damaged mucosa. The compounds used in the instant method therefore treat the high levels of acid in the stomach and allow the ulcer to heal.

(Office Action, pg. 2.)

Thus, as provided in the present specification, and as expressly recognized by the Office on the record, the specification does adequately described the claimed

subject matter. Accordingly, the premise that the application does not describe a "nexus between the modulation of urease activity and a useful treatment of a single disease or condition" is incorrect. For at least this reason, the rejections based thereon should be withdrawn.

iii) The claimed method of treating gastric mucosa injury is enabled

In support of the enablement rejection, the Office contends that "[t]he claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art . . . to make and/or use the invention." (Office Action, pg. 5.) In this regard, the Office Action further states that "[t]he specification does not specify what all is encompassed by gastric mucosa injury other than ulcers." (Office Action, pg. 7.) During the August 30, 2005, telephone conference, the Examiner confirmed that the allegedly non-enabled subject matter was the method of treating gastric mucosa injury. Applicant respectfully disagrees.

First, claims 11 and 12 specifically recite that the gastric mucosa injury comprises chronic gastritis or gastroduodenal ulcer, as expressly provided therein. Similarly, claims 17 - 20 specifically recite that the gastric mucosa injury comprises chronic gastritis or gastroduodenal ulcer, as expressly provided therein. Accordingly, at least with respect to these claims, the basis of the rejection, that "[t]he specification does not specify what all is encompassed by gastric mucosa injury other than ulcers" (Office Action, pg. 7), is inapplicable. For at least this reason, the enablement rejection of at least claims 11, 12, and 17-20 should be withdrawn.

Second, contrary to what is stated in the Office Action, the specification does provide guidance as to what is encompassed by gastric mucosa injury. For example,

page 18, lines 3-6 identify chronic gastritis and gastroduednal ulcer as within the scope of gastrointestinal diseases caused by urease of *H. Pylori.* Accordingly, with respect to all the claims, the basis of the rejection, that "[t]he specification does not specify what all is encompassed by gastric mucosa injury other than ulcers" (Office Action, pg. 7), is incorrect. For at least this reason, the enablement rejection should be withdrawn.

IV. REJECTION UNDER 35 U.S.C. § 102 OVER HIRAI

Claims 9-16 stand rejected under 35 U.S.C. § 102(b) over Hirai (JP04077476). Applicant respectfully traverses for the reasons of record and as further discussed below.

a. Summary of Applicant's Position

The rejection confounds the inherent properties of certain compounds with the inherency of the claimed method. The two are not the same. In particular, after citing the biological properties of certain compounds, the Office concludes that "the instant method claims are inherently taught by [Hirai]." (Office Action, pg. 3-4.) The question, however, is not what are the inherent properties of the claimed compound. Rather, the relevant question is whether the claimed *methods* are inherently disclosed by Hirai.[1]

The inherency-based rejection necessarily fails, however, because Hirai at most discloses the treatment of ulcers. Not all ulcers are caused by urease or *H.Pylori*, therefore Hirai does not inherently disclose treatment of gastric mucosa injury caused by urease or *H.Pylori*. The presently claimed methods are not inherent in Hirai's

[1] The inherency of the method can be the only basis for the present rejection, given that the Office has previously recognized that Hirai lacks any express teachings directed to methods of treating, *inter alia*, gastric mucosa injury caused by urease and/or *H.Pylori.*

treatment of ulcers or other conditions at least because, in the large number of ulcer patients not having Helicobacter pylori infection, the use of a compound according to Hirai would not **and cannot** provide urease inhibition or anti-Helicobacter pylori activity, and hence would not inherently treat gastric mucosa injury caused by urease or H.Pylori.

Further, claims 11, 17, and 19 are directed towards treating chronic gastritis, as more specifically set forth therein, and Hirai has not even been contended by the Office to teach or suggest a method of treating chronic gastritis, much less chronic gastritis caused by urease or H.Pylori.

b. It is Uncontested that not all Ulcers are Caused by Urease or *H.Pylori*

The fact that not all ulcers are caused by urease or *H.Pylori* is well documented and uncontested. Since an ulcer patient treated according to Hirai would not necessarily have an *H.Pylori* infection or gastric mucosa injury caused by urease, the treatment of this patent according to Hirai would not inherently treat gastric mucosa injury caused by urease or *H.Pylori*, as more specifically set forth in the claims.

As previously evidenced by Applicant on the record, gastrointestinal ulcers can be generally caused by a variety of conditions or factors, including:

1) infection with Helicobacter pylori,

2) use of non-steroidal anti-inflammatory drugs: NSAIDs (*e.g.,* aspirin),

3) unusually strong digestive activity with excess secretion of gastric acid, or

4) others (*e.g.*, stress).

Thus, all gastrointestinal ulcers are not caused by or associated with Helicobacter pylori infection. For this reason, the treatment of an ulcer generally, or more specifically, for example, an ulcer caused by NSAIDs, would not inherently be treating injury caused by urease or Helicobacter pylori infection, which are not present or associated with all ulcers.

c. Hirai is directed to treating uclers by reducing acid with a proton-pump inhibitor

Hirai does not teach (expressly or inherently) or suggest a method for treating gastric mucosa injury caused by urease or anti-Helicobacter pylori activity. To the contrary, the descriptions on treating ulcer are cited from Hirai as follows:

> 1) "It has been known that 2-[(3,5-dimethyl-4-methoxy-2-pyridyl)methylsulfinil]-5-methoxy-(1H)-benzimidazole (omeprazole) (a compound described in Japan kokai 54-141783) is clinically effective for suppressing gastric acid secretion as antiulcer agent by inhibiting H+, K+-adenosine triphosphatase (H+, K+ -ATP) which is an enzyme relating to the final stage of gastric acid secretion." (See Prior Art on page 4 of the English translation.)
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> 2) "The inventors made earnest studies on synthesis of benzisothiazolone derivatives and their pharmacological activity for years, consequently they discovered that the compounds of this invention have an enzymatic inhibition activity of H+, K+-adenosine triphosphatase over 100 times as much as that of above known omeprazole and become an excellent agent for preventing and treating ulcer, thus came to accomplish this invention." (See Problem to be Solved by the Invention on page 4 of the English translation.)
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> 3) "As described above, the compound (I) of this invention have excellent inhibitory action on H+, K+-ATPase and are useful for the prevention or treatment of gastrointestinal diseases, etc., of mankind, e.g., gastric

ulcer, duodenal ulcer, or Zollinger-Ellison syndrome, etc."
(See page 39 of English translation.)

Thus, Hirai simply and only discloses a method of preventing or treating gastrointestinal diseases caused by the above 3) ("inhibitory action on H+, K+-ATPase," *i.e.,* proton-pump inhibition) according to administration of the compound (I).

Hirai is silent about, among other things:

1. Treating gastrointestinal ulcer caused by infection with Helicobacter pylori;
2. Treating gastrointestinal ulcer caused by urease;
3. Treating chronic gastritis cause by Helicobacter pylori; and
4. Treating chronic gastritis cause by urease

d. *Helicobacter Pylori* Infections and ATPase Activity are Distinct

Practicing Hirai would not inherently be a treatment method as claimed. Indeed, it is generally considered that Helicobacter pylori is distinct from the ATPase activity of 3) above, and directly injures gastric mucosa or produce inflammatory-causing factor which brings about epithelium cell injuries on gastric mucosa.

For example, according to Huang, J.Q. et al., Lancent, 359:14-22, 2002 ("Huang") (attached to Applicant's June 20, 2005, Amendment) both Helicobacter pylori infection and NSAID use independently and significantly increase the risk of peptic ulcer and ulcer bleeding (Huang, pg. 14, col. 1, Interpretation.) While having Helicobacter pylori infection and taking NSAIDs increased the risk of bleeding ulcers,[2] a substantial portion of NSAID patients had ulcers in the absence of Helicobacter pylori infection.

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[2] The possibility that ulcer may be aggravated by both NSAIDs and Helicobacter pylori does change the fact that ulcers may be due to NSAIDs alone in the absence of Helicobacter pylori infection, and that the treatment of these ulcers is not (even inherently) a treatment of Helicobacter pylori infection or urease activity.

(Huang, pg. 14, col. 1, Findings, Interpretation.) Further, the contribution of NSAIDs is significant, since peptic ulcer disease was significantly more common in NSAID takers irrespective of Helicobacter pylori infection. (Huang, pg. 14, col. 1, Findings.) Huang also reports on the controversy of whether eradication of Helicobacter pylori infections retards ulcer healing in NSAID takers. (Huang, pg. 19, col. 2, - page 20, col. 1.)

The fact that use of NSAIDs results in peptic ulcer by a mechanism different from that of Helicobacter pylori infection is further shown in Wolfe, M.M. et al.: N. Engl. J. Med., 340:1888-1899, 1999 (attached to Applicant's June 20, 2005, Amendment), Wallace, J.L. et al.: Gastroenterology, 119:706-714, 2000 (attached to Applicant's June 20, 2005, Amendment), and Langenbach, R. et al.: Cell, 83:483-492, 1995 (attached to Applicant's June 20, 2005, Amendment).

e. There is no Legal or Factual Support for the Inherency-Based Rejection

In view of the above, as well as Applicants' previous remarks on the record, there is no support for the Office to maintain that Hirai inherently discloses a method of treating gastric mucosa injury by inhibition of urease or anti-Helicobacter pylori activity, as more specifically set forth in the claims. The reference simply does not teach (or even suggest) a method as claimed. Among other things, in the large number of ulcer patients that do not have Helicobacter pylori infection, the use of a compound according to Hirai would not and cannot inherently provide urease inhibition or anti-Helicobacter pylori activity.

Of course, to establish inherency, the evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference

...." Continental Can Co. USA, Inc. v. Monsanto Co., 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) (emphasis added). It is also well settled that "[i]nherency ... may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." Id. (internal citations omitted) (emphasis added). That is, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. Therefore, practicing Hirai on a ulcer patient generally, or a NSAID patent as specific example, would not be inherently practicing the claimed method because the patient would not necessarily have a Helicobacter pylori.

For at least the above reasons and those of record, reconsideration and withdrawal of the rejection are respectfully requested.

V. CONCLUSION

Applicant respectfully requests that this Amendment under 37 C.F.R. § 1.114 places claims 9-20 in condition for allowance. Applicant submits that new claims 17-20 do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner. Therefore, this Amendment should allow for immediate action by the Examiner.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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